AMENDMENTS TO THE SPECIFICATION:

On page 3, please replace paragraph [0007] with the following amended paragraph:

[0007] FSH is a heterodimeric hormone consisting of a 15 kDa ~~glycosylated~~ glucosylated α subunit and a 18 kDa ~~glycosylated~~ glucosylated β subunit. The dimeric structure is important for high affinity receptor binding and activation. The two subunits are tightly but noncovalently associated, and a discrete region with a concave surface, is thought to interact with FSHR. The FSH receptor belongs to a subfamily of glycoprotein hormone receptors within the G protein coupled receptor family. It comprises two halves of ~350 amino acids, the extracellular N-terminal exodomain and membrane associated c-terminal endodomain that includes 7 transmembrane helices. The exodomain binds the hormone with high affinity without hormone action. The exodomain/hormone complex undergoes a conformational change, and is thought to modulate the endodomain, thus generating a signal. Indeed, the entire extracellular domain undergoes a conformational change when introduced into a membrane mimicking detergent. Therefore, the high affinity interaction of the exodomain and FSH is the crucial first step leading to signal generation and hormone action. Despite the importance of this initial binding event, only limited information is available concerning the precise contact residues and sites in the exodomain as well as the hormone.

On page 8, please replace paragraph [0024] with the following amended paragraph:

[0024] In a further embodiment, the present invention is directed to a method of screening for compounds which modulate the interaction between CG and the exoloop 1, exoloop 2 or exoloop 3 domain on the LHR comprising: (a) attaching CG or a biologically active polypeptide fragment thereof to a substrate; (b) exposing CG or the biologically active polypeptide fragment thereof to an agent; and (c) determining whether said agent bound to CG or the biologically active polypeptide fragment thereof and further determining whether said agent modulates the

interaction between CG and the exoloop 1, exoloop 2 or exoloop 3 domain of the LHR. The present invention also contemplates a compound ~~indentified~~ identified by this method.

On page 56, please replace paragraph [00198] with the following amended paragraph:

[00198] FSH subunits could be separated on SDS-PAGE after deglycosylation with PNGase F (Fig. 9A, lane 2). It can be clearly seen that this procedure allows identification of the labeled upper band. Since the β subunit is larger than the ~~a~~ α subunit, the upper band was likely the β subunit. To clarify the identity of the upper band, deglycosylated FSH was electrophoresed and the gel was blotted on nitrocellulose membrane, then probed with antiFSH α and antiFSHβ antibodies. AntiFSHα antibody conspicuously labeled the lower band, whereas the antiFSH β antibody recognized primarily the upper band and faintly the lower band (Fig. 9B). These results show that the lower band represents the FSHα subunit whereas the upper band is the FSHβ subunit. The identity and specificity of the β subunit labeling are underscored by the remarkably contrasting labeling of the FSH α subunit by the FSHR exoloop 3 peptide.

On page 63, please replace paragraph [00209] with the following amended paragraph:

[00209] The FSH ~~αa~~ α and β subunits co-migrate on SDS-PAGE. To separate them on the gel FSH was deglycosylated with PNGase F and after it was photoaffinity labeled. Enzymatic cleavage was done by incubation of the labeled FSH complex with 20 or 50 units of PNGase F (New England BioLabs, Inc., MA) in 40 µl for 18 hours at 37°C. The samples were solubilized in SDS under the reducing condition and electrophoresed on 15 % gel containing 9 M urea.

On page 64, please replace paragraph [00211] with the following amended paragraph:

[00211] For easy comparison of the data, the ratios of Kd $^{\text{wild type/mutant}}$ ($Kd^{wt/mut}$), maximum $IPt^{mut/wt}$ and maximum $cAMP^{mut/wt}$ were calculated (Fig. 2B). The results show that all of the cells bound the hormone, indicating the surface expression of the mutant receptors. Of interest is that the L^{583} A and I^{584} A mutations improved the hormone binding affinity by 2-3 fold. This is in striking contrast to the loss of IP induction by most of the mutants except the V^{581} A and P^{582} A mutants. On the other hand, the mutational effect is less severe on the activation of adenylyl cyclase to produce cAMP. Most of the mutants were capable of producing some cAMP, although less than the wild type. The three mutants, L^{583} A, I^{584} A, and K^{590} A, did not produce cAMP. Therefore, the activation of PLCβ is more sensitive to Ala substitution than is the activation of AC and hormone binding. The results also show different mechanisms, in particular the sites, of the ~~PLCb~~ PLCβ activation, AC activation and hormone binding. We cannot, however, unequivocally dismiss the possibility that the lack of the IP induction was due to the limitation of the detectable ~~Ips~~ IPs. To visualize the difference, exoloop 3 was computer-modeled (Fig. 12A). The results showed the contrasting topography of the sensitive residues for the signal generation and hormone binding. The residues crucial for the PLCβ signal cover most of exoloop 3 except the N-terminal region (Fig. 12B). On the other hand, the residues sensitive to the AC signal are confined in the middle and C-terminus of the exoloop (Fig. 12C). L^{583} and I^{584} are most sensitive to hormone binding and are located near the middle of the exoloop (Fig. 12D). Their side chains protrude in opposite directions. The sensitive residues appear to be accessible from one side of the exoloop, suggesting the possibility that they might be modulated from the side of the exoloop by the exodomain and/or the hormone. Particularly, L^{583} and I^{584} are sensitive to all of the three functions: hormone binding, PLCβ activation and AC activation. In addition to L^{583} and I^{584}, K^{590} is important to the activation of PLCβ and AC.

On page 67, please replace paragraph [00215] with the following amended paragraph:

[00215] To determine whether the nature of the labeling, increasing concentrations of the hormone were labeled with a constant amount of ^{125}I-ABG-FSHR^{exo3}I (Fig. 17B). Conversely, increasing concentrations of ^{125}I-ABG-FSHR^{exo3}I were used to label a constant amount of FSH (Fig. 17C). The labeling plateaued under both conditions, indicating saturable labeling. To examine the relationship of the labeling with other exoloops and receptor peptide, FSH was incubated with in the presence of increasing concentrations of unlabeled FSHR peptides corresponding to exoloops 1, 2 and 3 as well as the N-terminal sequence S^{9}-K^{40}, FSHR$^{9-40}$, which is known to interact with FSH. Increasing concentrations of the peptides inhibited the photoaffinity labeling in a dose dependent manner and eventually blocked the labeling with varying affinity (Fig. 18), suggesting a specificity. FSHR^{exo2} is the most potent inhibitor, suggesting the possibility of its strong interaction with the hormone. Furthermore, failed to label denatured FSH hat does not bind to the receptor, despite high concentrations of the peptide (Fig. 19A), suggesting the specificity of the affinity labeling for biologically active FSH. FSH was denatured by boiling in 8M urea for 30 minutes. To test whether the denatured FSH remained in solution, the mixture of radioactively labeled FSH and unlabeled FSH was denatured, and varying volumes of the mixture were transferred to another tubes and the radioactivity was counted. The transfer was quantitative with a 99 - 100 efficiency, indicating denatured FSH was present in the photoaffinity labeling tube. ^{125}I-ABG-FSHR^{exo3}I did not label urokinase, phospholipases A, C and D (Fig. 19B). In addition, it failed to noticeably label human growth hormone (Fig. 19B). The exoloop 3 peptide inhibited ^{125}I-FSH binding to the receptor on intact cells in a dose dependent manner. These results show that the peptide's binding to and labeling of FSH were specific to bioactive FSH. Since the ~~a and b~~ α and β subunits of human FSH comigrate on SDS-PAGE, it is unclear which of the subunits was labeled. To determine the identity of the labeled subunit(s), FSH was labeled with ^{125}I-ABG-FSHR^{exo3}I, deglycosylated with PNGase F, and electrophoresed. The labeled band corresponded to the ~~a~~ α subunit (Fig. 19B). Deglycosylated human FSH separates into two bands on SDS-PAGE, the

higher molecular weight ~~b~~ β subunit in the upper band and the smaller ~~a~~ α subunit in the lower band, which was verified by monoclonal anti subunit antibodies.